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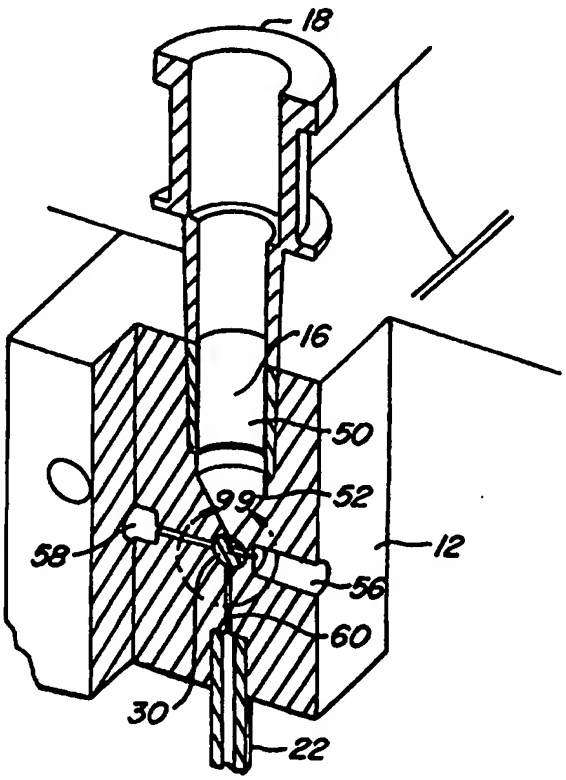
(54) **Title:** DEVICE AND METHODS FOR DISPENSING BEADS

(57) **Abstract**

The invention provides methods and apparatus for transporting articles held within a liquid medium from one location to another. Apparatus according to the invention comprises a hopper (16) having a top end, a bottom end (52), and at least one side wall (50) extending therebetween. The bottom end (52) includes an opening (54) therein, and the hopper (16) is adapted to receive the articles and the liquid medium. A means (58) is provided for injecting an amount of the liquid medium into the hopper to fluidize the articles while held within the liquid medium. The apparatus further includes a container (40) which may be aligned with the opening (54) at the bottom end (52) of the hopper (16). The container (40) is sized to receive a known quantity of at least one of the articles.



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DEVICE AND METHODS FOR DISPENSING BEADS

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation in part application of U.S. application Serial No. 08/555,799, filed November 9, 1995, the complete disclosure of which is herein incorporated by reference.

BACKGROUND OF THE INVENTION

This invention relates generally to the field of transporting articles, and more particularly to transporting very small articles which are held within a liquid medium. In one particular aspect, the invention relates to transporting beads on which diverse compounds have been synthesized.

Synthesizing processes where various compounds are placed on beads are described in, for example, U.S. Patent Application Serial Nos. 08/149,675, filed November 2, 1993 (Attorney Docket No. 16528J-004000) and 08/146,886, filed November 2, 1993 (Attorney Docket No. 16528J-000730), the disclosures of which are herein incorporated by reference. After synthesis, it is often desirable to analyze the compounds synthesized on the beads. One such process is by placing the beads in an assay solution and observing whether a positive result occurs. For analysis, the beads often need to be transported from one location to another. For example, in one such process groups of beads are initially placed into a plurality of wells where a portion of the compound on the beads is photo-chemically released. Assays are then performed on each well. For wells producing a positive result, the groups of beads are then transferred into another well or are further divided and placed into a plurality of wells so that further testing can occur to identify the compound.

When handling such beads, the beads are usually held within a liquid medium, such as water, to help prevent (among

other reasons) the beads from sticking together. Usually, such beads are very small, e.g. on the order of about 5 μm to 300 μm. Hence, transferring of such small beads from one location to another while held within a liquid medium is difficult and challenging. Transferring such small beads is especially challenging when a known quantity of beads, such as a single bead, must be individually transferred from a group of beads and placed in a test well.

It would therefore be desirable to provide methods and apparatus for transporting small articles from one location to another, particularly when the articles are held within a liquid medium.

SUMMARY OF THE INVENTION

The invention provides methods and apparatus for transporting articles from one location to another when the articles are held within a liquid medium. Apparatus according to the invention comprise a hopper having a top end, a bottom end having an opening therein, and at least one side wall extending between the top and bottom ends. The hopper is adapted to receive the articles and the liquid medium. A means is provided for injecting an amount of the liquid medium into the hopper to fluidize the articles while held within the liquid medium. The apparatus further includes a container which may be aligned with the opening at the bottom end of the hopper so that articles may exit the hopper from the opening and enter into the container. The container is sized to receive a known quantity of at least one of the articles. For example, the container may be sized and shaped to receive only a single article. Alternatively, the container may be sized and shaped to receive a specified range of articles at a time, such as, for example, 30 to 50 articles at a time.

In one preferable aspect, the hopper is tapered at the bottom end to assist in funneling the articles into the container. Preferably a vacuum source will be in communication with the container to assist in drawing the articles from the hopper and into the container. The apparatus preferably further includes a means for transferring

the articles from the container. In one particular aspect, the container includes an open top and a bottom having at least one opening therein, and the container is formed within a rotatable member. With such a configuration, the means for transferring comprises a pressure source and a fluid line in communication with the bottom of the container. In this manner, the pressure source may be employed to force an amount of liquid through the fluid line and the container to expel the article out of the top of the container after the container has been rotated out of alignment with the opening at the bottom end of the hopper. In another aspect, a motor is preferably provided to rotate the rotatable member to move the container in and out of alignment with the hopper. In still a further aspect, the hopper is formed within a housing having an aperture therein, with the rotatable member being rotatably held within the aperture. With such a configuration, the means for injecting comprises the pressure source which forces liquid between the rotatable member and the housing and into the hopper while expelling the article from the container.

In an alternative embodiment, the container comprises a lumen or a tube, and the means for transferring comprises a pressure source which forces an amount of the liquid through the tube to expel the article from the tube. In another aspect, the hopper and the container are formed within a housing, and the means for injecting comprises the pressure source which forces an amount of the liquid medium into the hopper when forcing the liquid medium through the tube to expel the article. In one aspect, the tube may be sized and shaped to receive only a single article at a time. In a further aspect, a means is provided for viewing articles as they are expelled from the tube.

In a further alternative embodiment, the means for transferring comprises a threaded shaft having grooves therein so that rotation of the shaft will move the article within the grooves and along the shaft. In another aspect, the means for transferring further comprises a pressure source which forces an amount of the liquid medium past the article to expel the

article. Preferably, the hopper is formed within a housing which includes an aperture for receiving the threaded shaft. The aperture includes an elongate slot along which the article is passed upon rotation of the threaded shaft. With such a configuration, the means for injecting preferably comprises the pressure source which forces an amount of the liquid medium through the elongate slot and into the hopper when expelling the article.

In a preferable aspect, the articles comprise beads. Usually, the beads are sized to be in the range from about 5 μm to 300 μm, more usually from about 10 μm to 200 μm. A plurality of test wells are preferably provided for receiving articles transported from the hopper. A translating mechanism may also be provided to translate the test wells so that a single well will receive the contents of the container each time the container is emptied. In a further aspect, a controller is provided for controlling pressure and vacuum provided by the pressure and vacuum sources. The controller is also in communication with the motor so that the controller may be employed to coordinate movement of the container with the pressure and vacuum. In still a further aspect, a hopper lid is provided for placement into the hopper. The hopper lid preferably includes at least one side wall which is sized and shaped to collect and trap bubbles existing on the hopper wall so that the bubbles will not attach to the articles and interfere with their dispersal from the hopper.

The invention provides an exemplary method for transporting articles held within a liquid medium. According to the method, the articles and the liquid medium are placed into a hopper having a bottom end having an opening therein. The articles are fluidized while within the hopper. A known quantity of at least one of the articles is funneled into a container positioned below and in alignment with the opening in the bottom end of the hopper. The article is then transferred from the container. In one aspect, the known quantity is a single article. Alternatively, the known quantity is a specified range of articles.

In one particularly preferable aspect, the container includes an open top and a bottom having at least one opening therein, and the transferring step comprises moving the container out of alignment with the opening in the bottom end of the hopper and forcing an amount of the liquid medium through the bottom of the container to expel the article. In another aspect, the container is formed within a rotatable member, and the rotatable member is rotated to move the container out of alignment with the opening in the bottom end of the hopper before the article is expelled.

In an alternative aspect, the container comprises a lumen or a tube, and the transferring step comprises forcing an amount of liquid through the tube to expel the article. Optionally, the article may be viewed as it is expelled from the tube. In still a further alternative aspect, the container comprises a groove in a threaded shaft, and the transferring step comprises rotating the shaft to move the at least one article along the shaft.

In one particular aspect, the fluidizing step comprises injecting an amount of the liquid medium into the hopper. Preferably, the liquid medium is injected through the bottom of the hopper. In yet another aspect, the hopper is tapered at the bottom end, and the funneling step comprises allowing the articles to settle within the hopper until the known quantity falls through the bottom of the hopper and into the container. Preferably, a vacuum will be created within the container to assist in drawing the known quantity from the hopper and into the container.

In still another aspect, the articles comprise beads having a size in the range from about 5 μm to 300 μm, more preferably from about 10 μm to 200 μm. Preferably, the liquid comprises water. In one particular aspect, the article is transferred to a test well. In still a further aspect, air bubbles which may exist on walls of the hopper are collected.

The invention further provides an exemplary apparatus for transporting articles and includes a reservoir for holding a plurality of articles that are preferably contained within a liquid medium. A paddle is disposed

beneath the reservoir and includes at least one hole extending therethrough. The hole is sized to receive a known quantity of at least one of the articles from the reservoir. A surface is disposed below the paddle and includes an aperture extending therethrough. The paddle is translatable relative to both the reservoir and the surface so that the hole may be aligned with the reservoir to receive the article from the reservoir (with the surface assisting to hold the article within the hole) and then translated into alignment with the aperture to allow the article to be transferred from the hole and into the aperture.

In a preferable aspect, the apparatus further includes a housing having a bottom end and sides which define a cavity. The housing is formed such that the aperture extends through the bottom end and the paddle is disposed above the bottom end. Further, the reservoir is formed within an insert which is received into the cavity above the paddle. In this manner, the paddle is sandwiched between the insert and the bottom end of the housing. With this arrangement, the hole in the paddle may easily be aligned with either the reservoir or the aperture by sliding the paddle within the cavity.

In one particular aspect, the insert includes a port which is aligned with the aperture in the bottom end. The port may function as a vent to allow the article to more easily be transferred from the hole and into the aperture. Optionally, the port may be configured to receive a fluid to flush the article from the hole and into the aperture.

In another aspect, the aperture includes multiple reservoirs and the paddle includes multiple holes which correspond to the number and arrangement of reservoirs. Further, the surface includes multiple apertures which correspond to the number and arrangement of holes. In this way, multiple articles may simultaneously be transferred into the apertures where they may be subsequently placed into a multi-well plate for analysis.

The invention still further provides an exemplary method for transferring articles. According to the method, a

plurality of articles are placed into a reservoir. A hole that is formed within a paddle is then aligned with the reservoir until a known quantity of at least one article is transferred into the hole. The paddle is then translated over a surface until the hole is aligned with an aperture within the surface. The article is then transferred from the hole into the aperture.

Preferably, the reservoir includes a liquid so that some of the liquid may be drained from the reservoir and into the hole to transfer the article. In one aspect, a vacuum may optionally be applied to the aperture to assist in transferring the article. In another option, a liquid may be flowed through the hole to assist in transferring the article from the hole and into the aperture.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is an isometric view of an exemplary apparatus for transporting articles held within a liquid medium according to the present invention.

Fig. 2 is an exploded view of the apparatus of Fig. 1.

Fig. 3, is a more detailed view of the apparatus of Fig. 2 taken along lines 3-3.

Fig. 4 is a perspective view of a rotatable member of the apparatus of Fig. 1.

Fig. 5 is a cross sectional side view of the rotatable member of Fig. 4.

Fig. 6 is a perspective view of an alternative embodiment of a rotatable member.

Fig. 7 is a cross sectional side view of the rotatable member of Fig. 6.

Fig. 8 is a cut-away perspective view of the apparatus of Fig. 1.

Fig. 9 is a more detailed view of the apparatus of Fig. 8 taken along lines 9-9.

Fig. 10 illustrates the apparatus of Fig. 9, with the rotatable member being rotated 180 degrees, such as when expelling an article.

Fig. 11 is a perspective view of an alternative embodiment of an apparatus for transporting articles held within a liquid medium according to the present invention.

Fig. 12 is a top view of the apparatus of Fig. 11.

Fig. 12A is a cross-sectional view of the apparatus of Fig. 12 taken along lines A-A.

Fig. 12B is a more detailed view of the apparatus of Fig. 12A taken along lines B-B.

Fig. 12C is a more detailed view of the apparatus of Fig. 12B taken along lines C-C.

Fig. 13 is a perspective view of a threaded shaft for use the apparatus of Fig. 11 according to the present invention.

Fig. 14 is a perspective view of a further alternative embodiment of an apparatus for transporting articles held within a liquid medium according to the present invention.

Fig. 15 is a top view of the apparatus of Fig. 14.

Fig. 15A is a cross-sectional view of the apparatus of Fig. 14 taken along lines A-A.

Fig. 15B is a more detailed view of the apparatus of Fig. 15A taken along lines B-B.

Fig. 15C is a more detailed view of the apparatus of Fig. 15B taken along lines C-C.

Fig. 16 is a cutaway sideview of an alternative embodiment of an apparatus for transferring articles showing a paddle having a hole, with the hole being aligned with a reservoir according to the invention.

Fig. 17 illustrates the apparatus of Fig. 16 with the paddle being translated to align the hole with an exit aperture according to the invention.

Fig. 18 is a top view of the apparatus of Fig. 16.

Fig. 19 is a perspective view of a housing of the apparatus of Fig. 16.

Fig. 20 is a top view of the housing of Fig. 19 showing the exit aperture formed in a bottom end.

Fig. 21 is a top view of the paddle of Fig. 16.

Fig. 22 is a top view of an insert having the reservoir of the apparatus of Fig. 16.

Fig. 23 is a top view of an alternative paddle having a two-dimensional array of holes for receiving articles according to the invention.

DETAILED DESCRIPTION OF THE SPECIFIC EMBODIMENTS

The invention provides methods and apparatus for transporting articles from one location to another while held within a liquid medium. Articles transported by the invention will be small, typically on the order of 5 μm to 300 μm, more usually from about 80 μm to 200 μm. The articles will usually comprise beads on which various compounds have been synthesized, such as by the processes described in U.S. Patent Application Serial Nos. 08/149,675 and 08/146,886, previously incorporated by reference. The beads are usually constructed of a polymer such as polystyrene and polyethylene glycol. Such beads are commercially available from, for example, Nova Bio-chem.

Such beads will often be stored and transported while within a liquid medium, such as water, ethanol, methanol, buffer, DMSO, and the like. Such a liquid medium will preferably be less dense than the beads so that the beads will settle and sink within the medium. Among other reasons, the liquid medium helps prevent the beads from sticking or clumping together.

The methods and apparatus will be configured to transport a known quantity of articles. For instance, a single article may be removed from a larger group and individually transported to another location. Alternatively, a smaller group of a known quantity, e.g. about 30-50, may be removed from a larger group and transported to another location.

To transport the articles, the articles (while within the liquid medium) will preferably be placed into a hopper having an opening at a bottom end. Preferably, the hopper will be tapered at the bottom end so that the articles will tend to settle toward the opening. To assist in a

uniform settlement of the articles within the hopper, the articles will preferably be fluidized. By fluidizing it is meant that the articles will be separated from each other while within the liquid medium so that as the articles settle within the hopper, they will tend to uniformly settle within the tapered end, without clumping together or forming a bridge across the bottom end to prevent any articles from exiting the bottom end. Usually, the articles will be fluidized by injecting an amount of the liquid medium into the hopper, preferably from the bottom end. Such a configuration is further advantageous in that it helps to insure that all articles will be dispensed from the hopper.

As the articles settle, they will fall from the hopper and into a container. Preferably, a vacuum will be provided to assist in drawing the articles out of the hopper. The container will preferably be sized to receive the known quantity of the articles. In this manner, the size of the container may be employed to assist in regulating the number of articles which are dispensed from the hopper at a time. After the container is filled with the known quantity, the container will be emptied and the remaining articles within the hopper will once again be fluidized so that the process may be repeated.

Referring now to Fig. 1, an exemplary apparatus 10 for transporting beads held within a liquid medium will be described. The apparatus 10 includes a housing 12 that is removably attached to a frame 14. Formed within housing 12 is a hopper 16 into which beads and a liquid medium are initially placed. A lid 18 is further provided and is slidable within the hopper 16. The apparatus 10 further includes a motor 20 which rotates a rotatable member (not shown) which in turn distributes the beads from the hopper 16 as described in greater detail hereinafter. Extending from housing 12 is a tube 22 through which dispensed beads are delivered to wells 24 of a multi-well plate 26. A translating mechanism 28 is provided which translates plate 26 so that each of the wells 24 may be separately aligned with tube 22 each time a known quantity of beads is distributed from the hopper 16.

Referring to Figs. 2 and 3, construction of the apparatus 10 will be described in greater detail. Apparatus 10 further includes a rotatable member 30 having a proximal end 32 and distal end 34. Proximal end 32 extends through an aperture 36 in frame 14 where it is operably attached to a shaft 38 by a coupler (not shown) on motor 20. In this way, actuation of the motor 20 will cause rotatable member 30 to rotate.

Distal end 34 of rotatable member 30 is received within housing 12. Distal end 34 includes a container 40 which may be aligned with hopper 16 when rotatable member 30 is received within housing 12. Housing 12 and rotatable member 30 will preferably be constructed of a substantially transparent material, such as polycarbonate, so that the transfer of beads may be visualized. Visualization may be provided be employing a sensor, such as a laser sensor, or by image processing. In this manner, the transfer of beads from hopper 16 to container 40 may be confirmed. Alternatively, housing 12 and rotatable member 30 may be constructed of other, non-transparent materials.

Referring to Figs. 4 and 5, construction of rotatable member 30 will be described in greater detail. Container 40 is integrally formed within distal end 34 and is generally cylindrical in geometry (although other configurations are possible). Container 40 includes an open top end 42 and a bottom end 44 having an aperture therein. Ninety degrees from container 40 is a lumen 46 which is in communication with container 40 via a passage 48. As described in greater detail hereinafter, a vacuum or a pressure source may be placed in communication with lumen 46 to assist in drawing beads into container 40 or expelling them therefrom. Container 40 is preferably sized so that it will receive only a single bead at a time. In this manner, individual dispensing of beads from hopper 16 can be controlled by the size of container 40.

Shown in Figs. 6 and 7 is an alternative embodiment of a rotatable member 30'. Rotatable member 30' is essentially identical to rotatable member 30 except for the

configuration of distal end 34'. In rotatable member 30', container 40' is sized to receive a specific range of beads, e.g. 30 to 50 at a time. Since container 40' is larger than container 40, a plurality of passages 48' are provided to connect container 40' with lumen 46'. In this way, higher flow rate of fluid through container 40' is attained.

Referring to Fig. 8, construction of housing 12 will be described in greater detail. Hopper 16 is integrally formed within housing 12 and has a generally cylindrical portion 50 and a generally cone-shaped bottom portion 52. As best shown in Fig. 9, bottom portion 52 includes an aperture 54 having a size which generally matches the size of open top 42 of container 40. The cone-shaped geometry of bottom portion 52 is advantageous in that it assists in funneling beads toward aperture 54 and into container 40.

Also formed within housing 12 is a vacuum port 56 and a pressure port 58. A vacuum source (not shown) will be connected to vacuum port 56 to assist in drawing beads from hopper 16 and into container 40. Pressure port 58 will be connected to a pressure source (not shown) which will serve to both fluidize the beads within hopper 16 and to assist in expelling beads from container 40.

Referring to Fig. 9, operation of apparatus 10 to dispense a bead (or a known quantity of beads) from hopper 16 will be described. Initially, hopper 16 is filled with beads and a liquid medium. Rotatable member 30 will be positioned to align container 40 with aperture 54. In this position, lumen 46 is aligned with vacuum port 56 as shown. A vacuum is then applied to vacuum port 56 to help draw one of the beads from hopper 16 into container 40. Passage 48 will be small enough so that a bead will be prevented from entering therein. After the bead is dispensed into container 40, rotatable member 30 is rotated 180° to the position shown in Fig. 10. In Fig. 10, container 40 is aligned with a lumen 60 which empties into tube 22 (see Fig. 8). In this position, lumen 46 of rotatable member 30 is aligned with pressure port 58. At this point, pressurized fluid is introduced through pressure port 58 to force fluid through lumen 46, passage 48, and

container 40. The pressurized fluid expels the bead from container 40 and into lumen 60 where it passes into tube 22. From there, the dispensed bead will be placed into a well 24 of plate 26.

The tolerance between rotatable member 30 and housing 12 will be such that when pressurized fluid is forced through pressure port 58, some of the fluid will pass between housing 12 and rotatable member 30 and into hopper 16. In this manner, pressurized fluid will be forced upwardly through hopper 16 to fluidize the beads therein. Such fluidization prevents the beads in hopper 16 from clumping together or from forming bridges within bottom portion 15 which may prevent dispensing of beads through aperture 54. After fluidization, the beads settle uniformly within bottom portion 52 so that a single bead will be able to be dispensed through aperture 54. After the bead has been dispensed from container 40, rotatable member 30 is rotated 180° back to the position shown in Fig. 9 and the process is repeated. Preferably, a controller or microprocessor (not shown) will be provided to coordinate rotation of rotatable member 30 with the application of the vacuum and introduction of the pressurized fluid.

Referring back to Fig. 8, lid 18 will preferably be constructed such that a small tolerance will exist between lid 18 and hopper 16 when lid 18 is inserted therein. As lid 18 is pushed into hopper 16, air bubbles on the hopper walls will be trapped and collected by lid 18. In this way, undesirable attachment of the beads to the air bubbles will be prevented. Optionally, lid 18 may be constructed to be an extension of housing 12.

Referring to Figs. 11-13, an alternative embodiment of a housing 62 which may be used with apparatus 10 will be described. As best shown in Fig. 12B, housing 62 includes a hopper 64 having a cone-shaped bottom portion 66. As best shown in Fig. 12C, a container 68 is formed in housing 62 and is open to bottom portion 66. Container 68 is preferably sized to receive only a single bead at a time. Container 68 is also open to an elongate cylindrical opening 70 formed in housing 62. An elongate groove 72 is also formed in housing

62 and is open to both cylindrical opening 70 and container 68. Cylindrical opening 70 is sized and shaped to receive an elongate threaded shaft 74 as shown in Fig. 13.

With threaded shaft 74 in opening 70, a bead may be dispensed from hopper 64 as follows. Initially, a vacuum is applied from a vacuum port 76 in housing 62 which assists in drawing a bead from bottom portion 66 into container 68. As the bead settles into container 68, a portion of the bead sits within the threads of shaft 74. Shaft 74 is then rotated (such as by motor 20) to translate the bead along groove 72. When the bead reaches the end of groove 72, pressurized liquid is introduced through a pressure port 78 which moves the bead from housing 62 through vacuum port 76. From vacuum port 76, the bead may be delivered to a test well. Introduction of pressurized liquid through port 78 also serves to fluidize beads within hopper 64. Specifically, some of the liquid passes through groove 72, into container 68, and upward into bottom portion 66. After fluidization, container 68 may be refilled with another bead and the process repeated.

Referring to Figs. 14, 15, and 15A-15C, another alternative embodiment of a housing 80 that may be used with apparatus 10 will be described. As best shown in Fig. 15B, housing 80 includes a hopper 82 having a generally cone-shaped bottom portion 84. Bottom portion 84 empties into a container 86. Container 86 is preferably cylindrical in geometry and has a diameter sized such that only a single bead can enter therein at a time. Housing 80 includes an exit port 88 and a pressure port 90. Ports 88 and 90 are in communication with the container 86 and assist in dispensing beads from hopper 82 as follows. Initially, with the assistance of gravity, a bead is drawn from bottom portion 84 into container 86. As a bead enters container 86, pressurized fluid is introduced through port 90 to force the bead from container 86 and into exit port 88 where it may be dispensed into a test well. As best shown in Fig. 15C, exit port 88 is at atmospheric pressure so that pressurized fluid from port 90 will force the bead into port 88. At the same time, some of the pressurized fluid will be forced into bottom portion 84 to fluidize the articles held

therein. After fluidization, the beads are allowed to settle and one will drop into container 86 and out through exit port 88. A sensor, such as a laser sensor, may be employed to confirm placement of a bead into the container 86.

Referring now to Figs. 16 and 18-22, an alternative embodiment of an apparatus 100 for transferring articles will be described. Apparatus 100 comprises a housing 102 having a bottom end 104 and sides 106 which define a cavity 108 (see Fig. 19). Formed within bottom end 104 is an exit aperture 110 which allows articles to be transferred from housing 102 into a test well for analysis as described in greater detail hereinafter. Although shown to be tapered, exit aperture 110 may be straight-sided or be constructed of a length of tubing.

Positioned above bottom end 104 is a paddle 112 which includes a hole 114 extending therethrough. Paddle 112 is received into cavity 108 and can be translated back and forth by manipulating a handle 116. As best shown in Figs. 18 and 19, handle 116 extends through a slot 118 within housing 102 to allow paddle 112 to be translated within cavity 108. As shown in Fig. 21, paddle 112 includes steps 120 which engage side 106 of housing 102 to limit the travel of paddle 112 when translated.

Disposed above paddle 112 is an insert 122. Insert 122 includes a reservoir 124 for holding a plurality of articles which are to be sorted and transferred as described in greater detail hereinafter. Although shown to be tapered, reservoir 124 may be straight-sided or even a single piece of tubing to facilitate transfer of the beads from the reservoir 124 into hole 114. Insert 122 further includes a port 126. Port 126 is aligned with exit aperture 110 (see Fig. 16) and assists in transferring beads from hole 114 to aperture 110 as described in greater detail hereinafter. A pair of leaf springs 128 (see Fig. 18) are provided to secure insert 122 within cavity 108.

As shown in Fig. 16, paddle 112 is positioned within cavity 108 so that hole 114 is aligned with reservoir 124. In this manner, beads held within reservoir 124 will fall with the assistance of gravity into hole 114. Preferably,

reservoir 124 will also include a liquid medium into which the beads are placed. In this way, when hole 114 is aligned with reservoir 124, the beads will tend to settle within the liquid medium until they come to rest within hole 114. Preferably, hole 114 will be primed and filled with a liquid sc that no air bubbles will exist within hole 114.

Hole 114 will preferably be sized such that a known quantity of beads may be received therein. For example, hole 114 may be configured to receive one, ten, one hundred or even more beads at a time. Further, paddle 112 will preferably be configured to have a height which corresponds to the height of a single layer of beads. This arrangement allows for a more uniform filling of hole 114 and easier transfer into aperture 110.

As shown in Fig. 17, once a known quantity of beads has been transferred into hole 114, handle 116 is pulled backward to slide paddle 112 within cavity 108 until hole 114 is aligned with exit aperture 110. When aligned with exit aperture 110, steps 120 will preferably engage side 106 to prevent further translation of paddle 112. During translation, bottom end 104 of housing 102 maintains the beads within hole 114. Upon alignment, beads 114 fall with the assistance of gravity into exit aperture 110 where they will exit housing 102. Port 126 may serve as a vent to assist in the transfer of the beads into aperture 110. Optionally, a liquid may be flowed through port 126 to help wash beads from hole 114. In a further alternative, a vacuum may be applied to aperture 110 to assist in transferring the beads from hole 114.

Referring now to Fig. 23, an alternative embodiment of a paddle 130 will be described. Paddle 130 includes ninety-six holes 132 which may be configured essentially identical to hole 114 as previously described. Paddle 132 is configured to be used with an apparatus that is similar to apparatus 100 but includes multiple reservoirs and exit apertures which will correspond to holes 132. In this manner, ninety-six sets of beads may simultaneously be transferred. Such a configuration is advantageous in that the wells of a

standard sized microplate may be filled with sets of beads upon translation of paddle 132 in a manner analogous to that previously described in connection with Figs. 16 and 17. In this way, multiple test wells may each be filled with a known quantity of beads so that analysis of the compounds on the beads may be performed in a rapid and efficient manner.

The invention has now been described in considerable detail for purposes of understanding. However, alternative uses for the invention will occur to those of skill in the art. Therefore, the above description should not be taken as limiting the scope of the invention. Instead, the scope of the invention should be determined chiefly with reference to the appended claims, along with a full scope of equivalents to which those claims are entitled.

WHAT IS CLAIMED IS:

1. A method for transporting articles held within a liquid medium, the method comprising:

placing the articles and the liquid medium into a hopper having a bottom end with an opening therein;

fluidizing the articles while within the hopper;

funneling a known quantity of at least one of the articles into a container positioned below and in alignment with the opening in the bottom end of the hopper; and

transferring the at least one article from the container.

2. A method as in claim 1 or 22, wherein the known quantity is a single article or a specified range of articles, and wherein the articles comprise beads having a size in the range from about 5 μm to 300 μm.

3. A method as in claim 1, wherein the container includes an open top and a bottom having at least one opening therein, wherein the transferring step comprises moving the container out of alignment with the opening in the bottom end of the hopper and forcing an amount of a liquid through the bottom of the container to expel the at least one article, wherein the container is formed within a rotatable member, and wherein the rotatable member is rotated to move the container out of alignment with the opening in the bottom end of the hopper before the at least one article is expelled.

4. A method as in claim 1, wherein the container comprises a tube, and wherein the transferring step comprises forcing an amount of liquid through the tube to expel the at least one article, and further comprising viewing the article as it is expelled from the tube.

5. A method as in claim 1, wherein the container comprises a groove in a threaded shaft, and wherein the

transferring step comprises rotating the shaft to move the at least one article along the shaft.

6. A method as in claim 1, wherein the fluidizing step comprises injecting an amount of the liquid medium into the hopper, wherein the liquid medium is injected through the bottom of the hopper, wherein the hopper is tapered at the bottom end, wherein the funneling step comprises allowing the articles to settle within the hopper until the known quantity falls through the bottom of the hopper and into the container, and, wherein the funneling step further comprises creating a vacuum within the container to assist in drawing the known quantity into the container.

7. An apparatus for transporting articles held within a liquid medium, the apparatus comprising:

a hopper having a top end, a bottom end, and at least one side wall extending therebetween, the bottom end having an opening therein, wherein the hopper is adapted to receive the articles and the liquid medium;

means for injecting an amount of the liquid medium into the hopper to fluidize the articles while held within the liquid medium; and

a container which may be aligned with the opening at the bottom end of the hopper, wherein the container is sized to receive a known quantity of at least one of the articles.

8. An apparatus as in claim 7, wherein the hopper is tapered at the bottom end, further comprising means for transferring the articles from the container, wherein the container includes an open top and a bottom having at least one opening therein, wherein the container is formed within a rotatable member, and wherein the means for transferring comprises a pressure source and a fluid line in communication with the bottom of the container, wherein the pressure source forces an amount of the liquid through the fluid line and the container to expel the at least one article out of the top of

the container after the container is rotated out of alignment with the opening at the bottom end of the hopper.

9. An apparatus as in claim 8, further comprising a motor which rotates the rotatable member, wherein the hopper is formed within a housing, wherein the housing includes an aperture having the rotatable member rotatably held therein, and wherein the means for injecting comprises the pressure source which forces liquid between the rotatable member and the housing and into the hopper while expelling the at least one article from the container.

10. An apparatus as in claim 7, wherein the container is sized and shaped to receive only a single article or a specified range of articles at a time.

11. An apparatus as in claim 7, wherein the container comprises a tube, and further comprising a pressure source which forces an amount of liquid through the tube to expel the at least one article from the tube, wherein the hopper and the container are formed within a housing, wherein the means for injecting comprises the pressure source which forces an amount of the liquid medium into the hopper when forcing the liquid medium through the tube to expel the article, wherein the tube is sized and shaped to receive only a single article at a time, and further comprising means for viewing articles as they are expelled from the tube.

12. An apparatus as in claim 7, further comprising a threaded shaft having grooves therein so that rotation of the shaft will move the at least one article within the grooves and along the shaft to transfer the article from the container, a pressure source which forces an amount of the liquid medium past the at least one article to expel the at least one article, and a vacuum source which draws an amount of the liquid medium past the at least one article to expel the at least one article.

13. An apparatus as in claim 12, wherein the hopper is formed within a housing, wherein the housing includes an aperture for receiving the threaded shaft, wherein the aperture includes an elongate slot along which the at least one article is passed upon rotation of the threaded shaft, and wherein the means for injecting comprises the pressure source which forces an amount of the liquid medium through the elongate slot and into the hopper when expelling the at least one article.

14. An apparatus as in claim 7, wherein the articles comprise beads which are sized in the range from 5 μm to 300 μm, further comprising a plurality of test wells for receiving articles transported from the hopper, and further comprising a translating mechanism which translates the test wells so that a single well will receive the contents of the container each time the container is emptied.

15. An apparatus as in claim 7, further comprising a vacuum source in communication with the container which assists in drawing the known quantity into the container, wherein the means for injecting comprises a pressure source, and further comprising a controller which controls pressure or vacuum delivery, and wherein the controller coordinates movement of the container with pressure or vacuum delivery.

16. An apparatus as in claim 7, further comprising a hopper lid which may be placed over the top of the hopper, wherein the hopper lid includes at least one side wall which is sized and shaped to collect and trap bubbles existing on the hopper wall.

17. An apparatus for transporting articles, the apparatus comprising:

a reservoir for holding a plurality of articles contained within a liquid medium;

a paddle having at least one hole extending therethrough, the hole being sized to receive a known quantity

of at least one of the articles from the reservoir, wherein the paddle is disposed below the reservoir; and

a surface disposed below the paddle, the surface having an aperture extending therethrough;

wherein the paddle is translatable relative to both the reservoir and the surface so that the hole may be aligned with the reservoir to receive the article from the reservoir and then translated into alignment with the aperture to allow the article to be transferred from the hole and into the aperture.

18. An apparatus as in claim 17, further comprising a housing having a bottom end and sides which define a cavity, wherein the aperture extends through the bottom end, wherein the paddle is disposed above the bottom end, and wherein the reservoir is formed within an insert which is received into the cavity above the paddle.

19. An apparatus as in claim 18, wherein the insert includes a port which is axially aligned with the aperture in the bottom end.

20. An apparatus as in claim 17, wherein the known quantity is a single article or a specified number of articles.

21. An apparatus as in claim 17, further comprising multiple reservoirs, wherein the paddle includes multiple holes which correspond to the number and arrangement of reservoirs, and wherein the surface includes multiple apertures which correspond to the number and arrangement of holes, whereby multiple articles may be simultaneously dispensed.

22. A method for transferring articles, the method comprising:

placing a plurality of articles into a reservoir;

aligning a hole that is formed within a paddle with the reservoir until a known quantity of at least one article is transferred into the hole;

translating the paddle over a surface until the hole is aligned with an aperture within the surface and transferring the article from the hole and into the aperture.

23. A method as in claim 22, wherein the reservoir includes a liquid, and further comprising draining at least some of the liquid from the reservoir and into the hole to transfer the article.

24. A method as in claim 22, applying a vacuum to the aperture to assist in transferring the article from the hole and into the aperture.

25. A method as in claim 22, further comprising flowing a liquid through the hole to assist in transferring the article from the hole and into the aperture.

26. A method as in claim 22, further comprising transferring the article from the aperture to a test well.

27. A method as in claim 22, further comprising transferring articles from multiple reservoirs into multiple holes within the paddle.

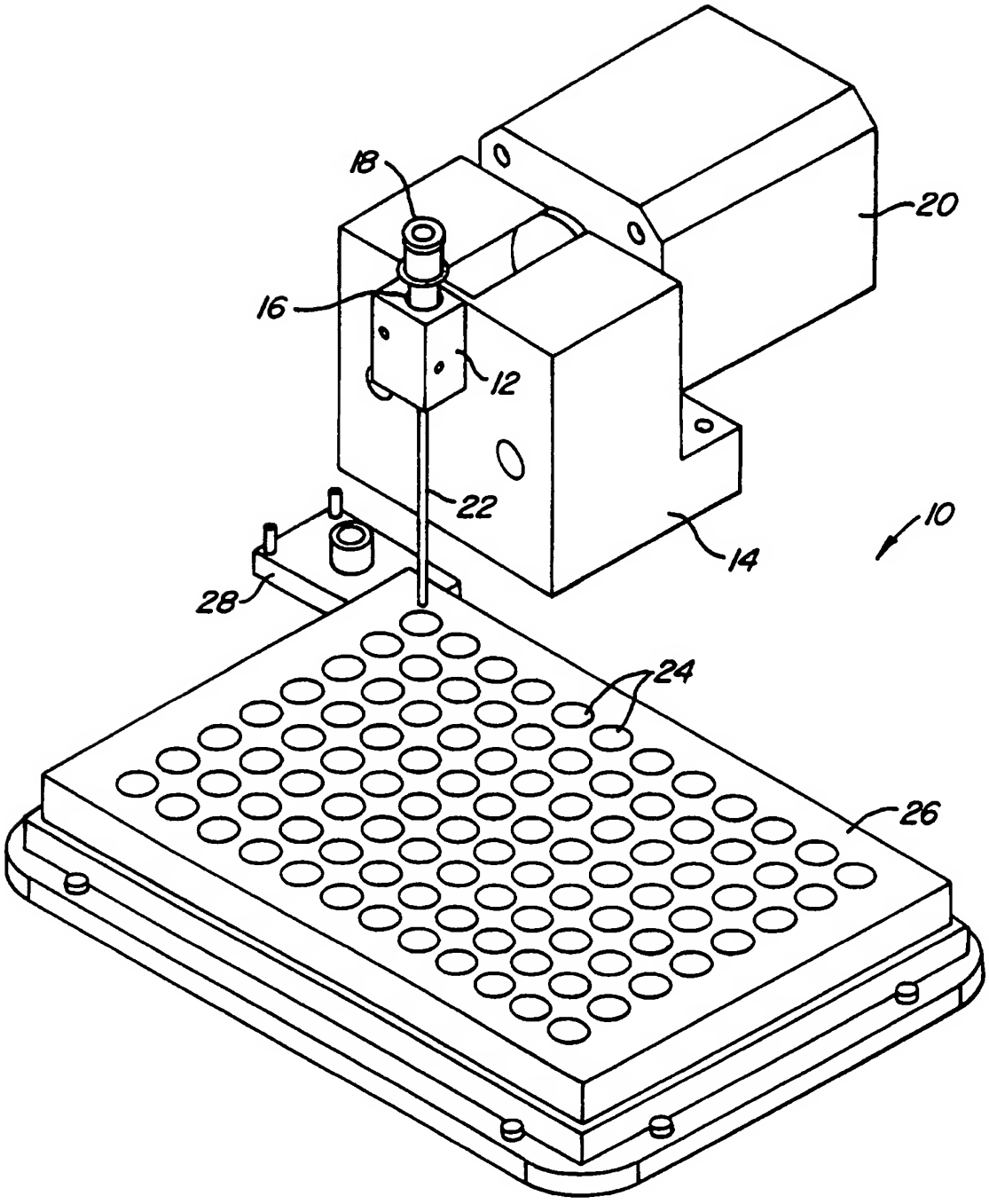

FIG. 1.

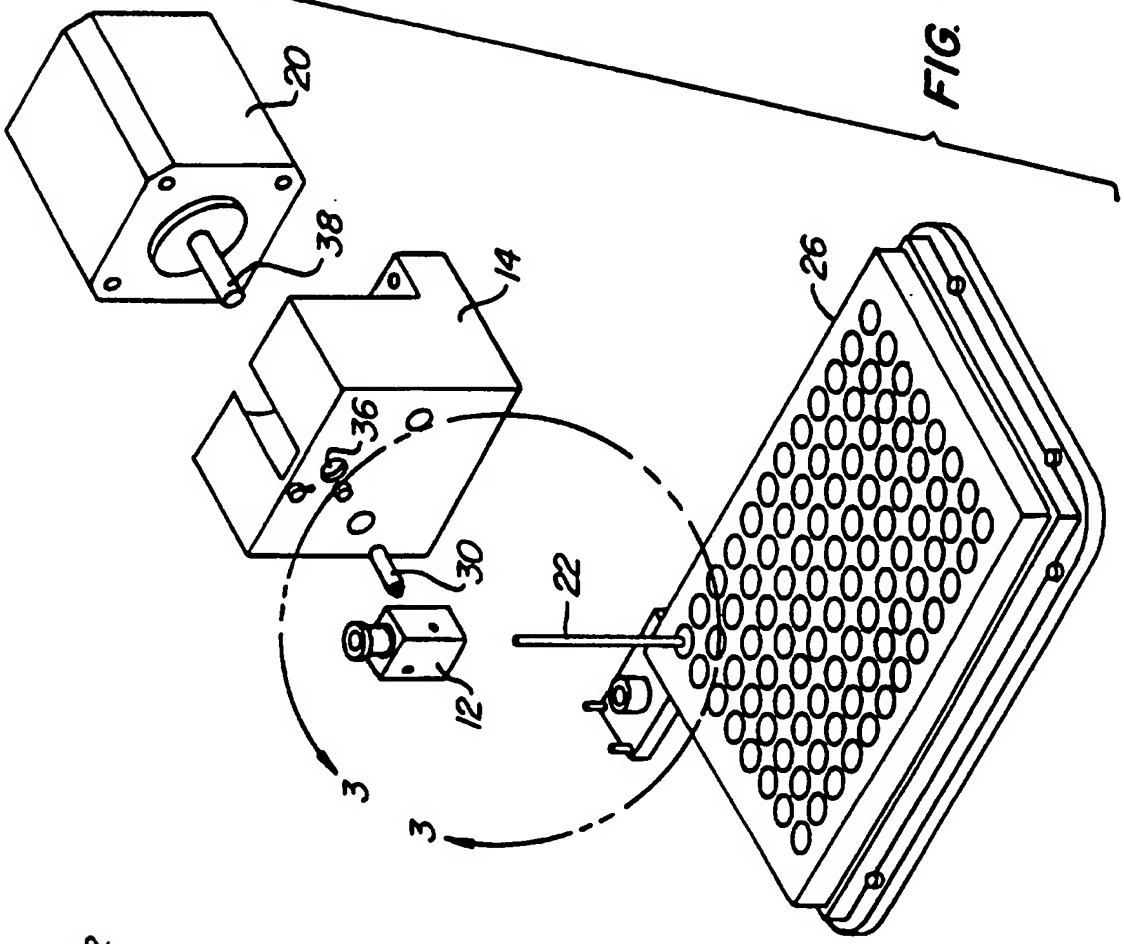

FIG. 2.

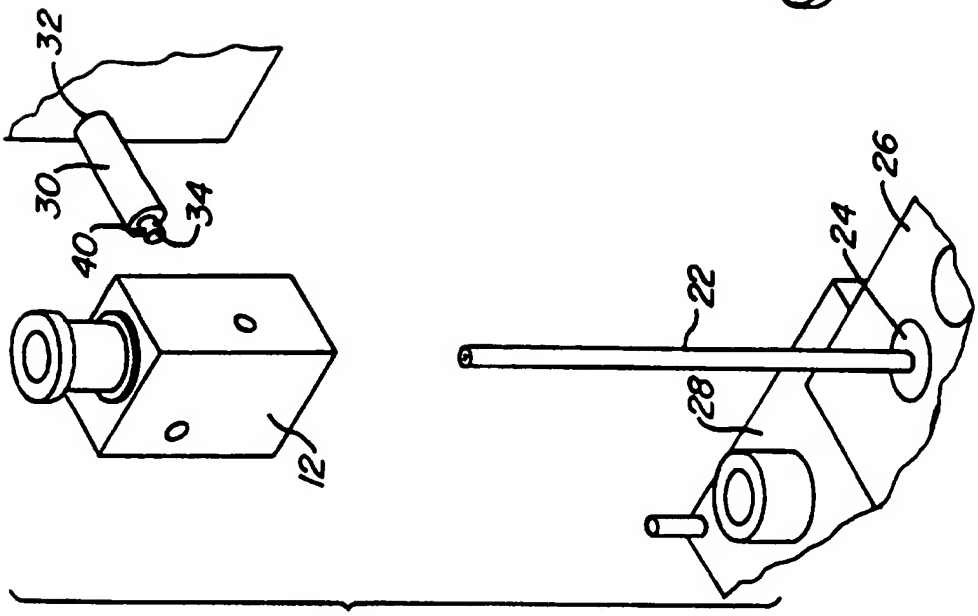

FIG. 3.

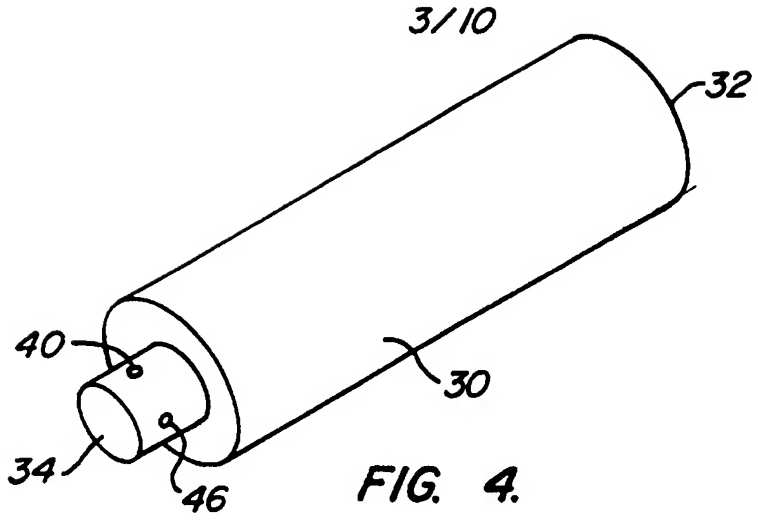

FIG. 4.

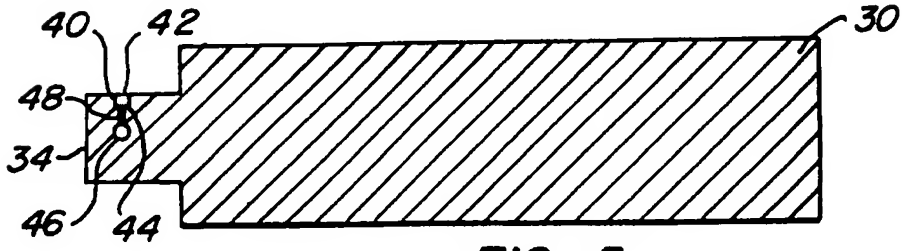

FIG. 5.

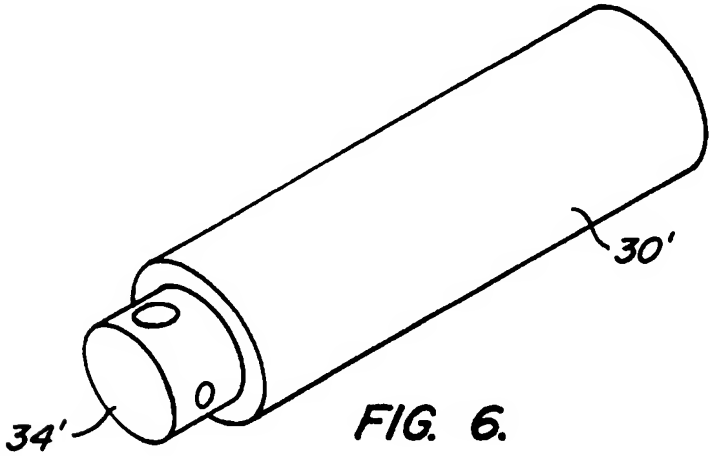

FIG. 6.

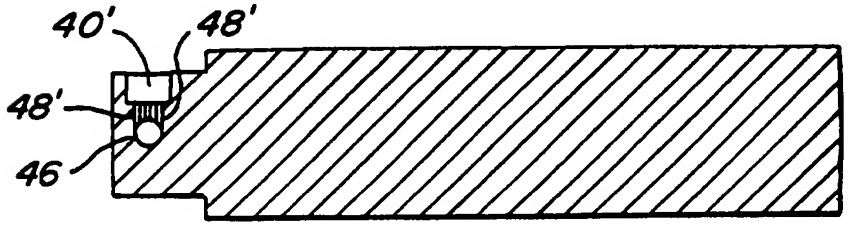

FIG. 7.

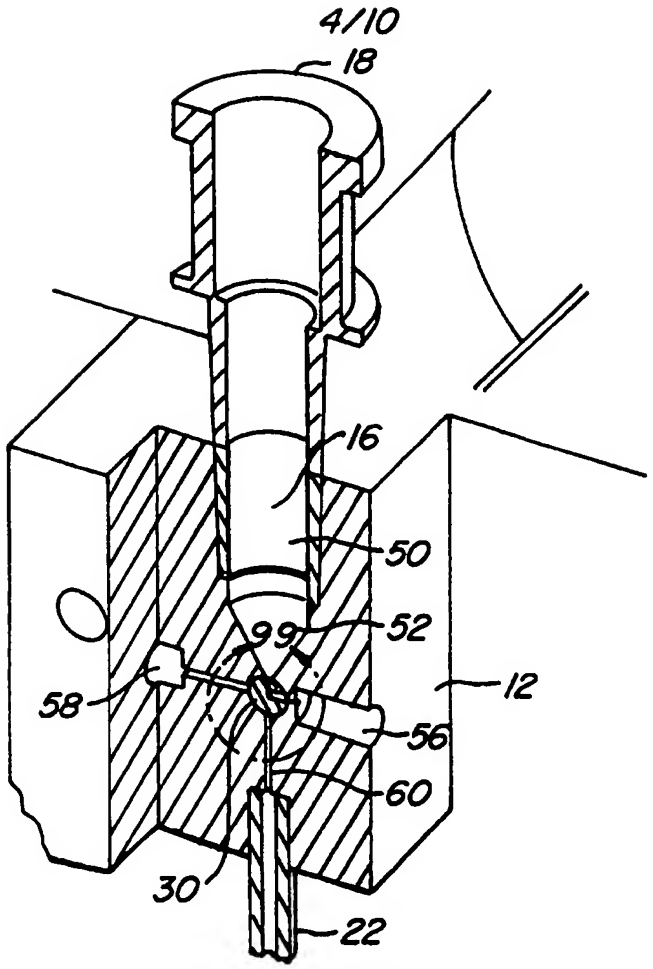

FIG. 8.

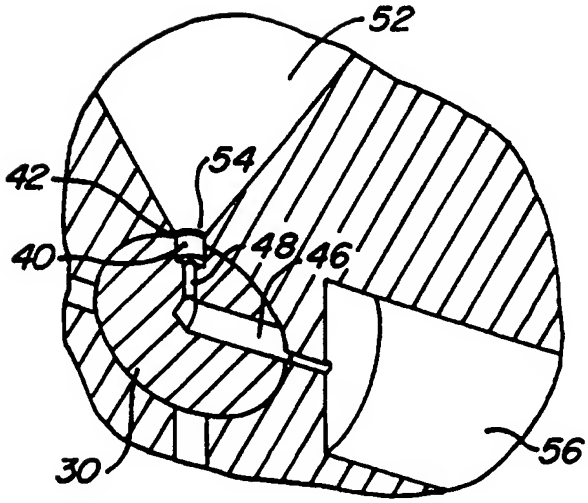

FIG. 9.

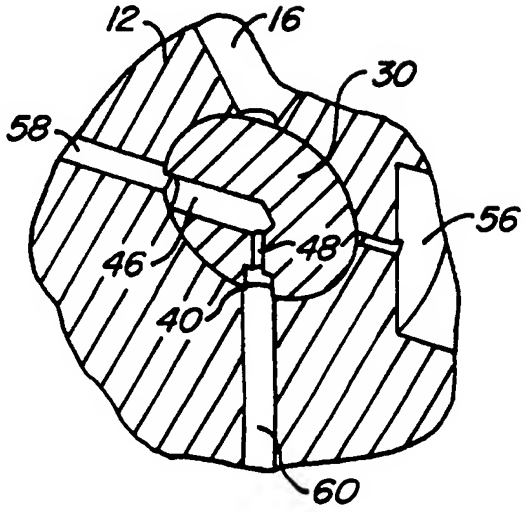

FIG. 10.

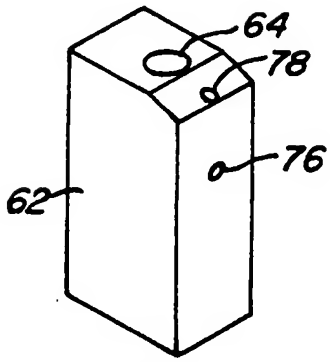

FIG. 11.

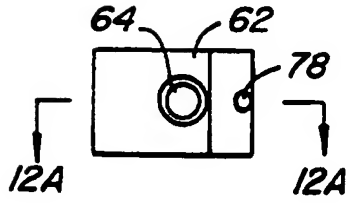

FIG. 12.

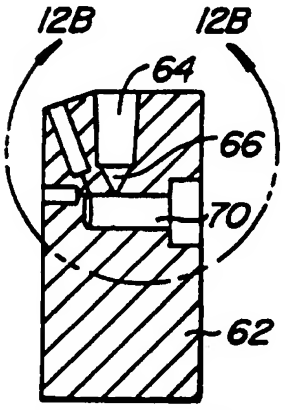

FIG. 12A.

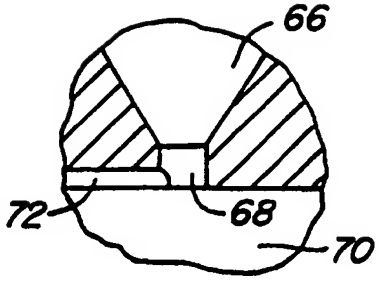

FIG. 12C.

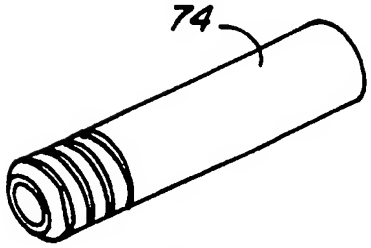

FIG. 13.

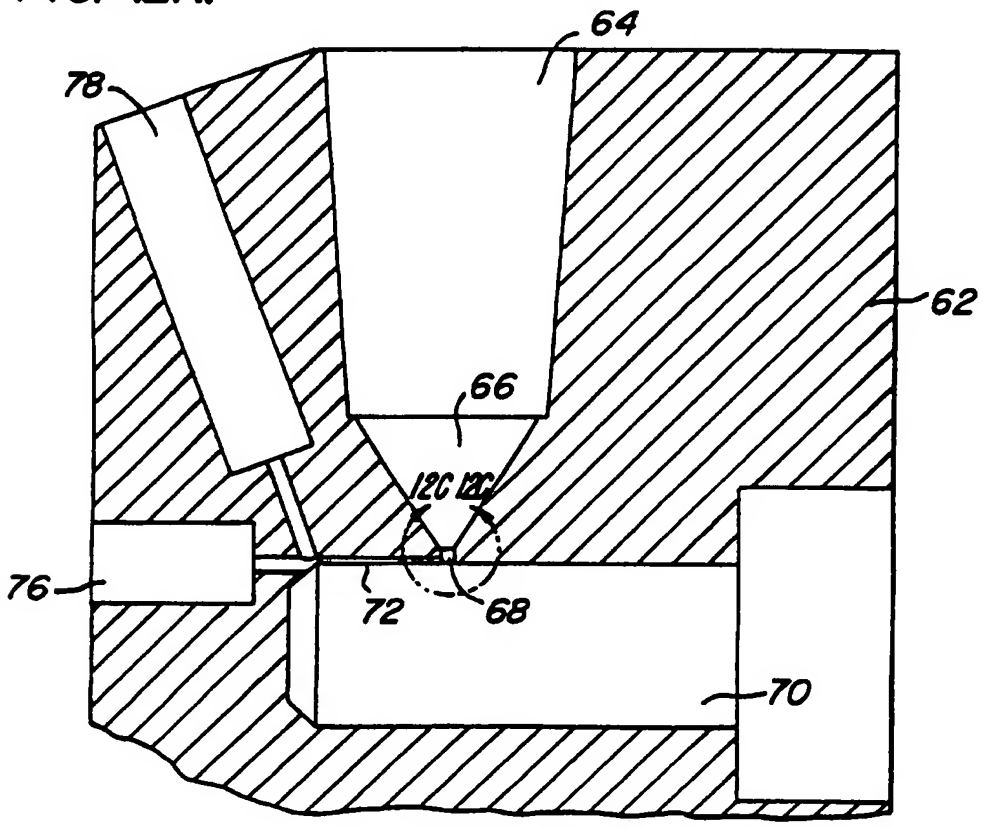

FIG. 12B.

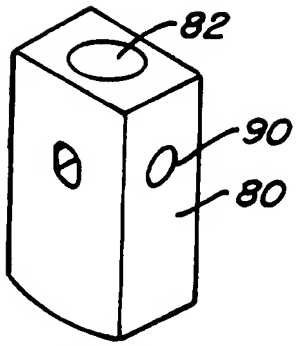

FIG. 14.

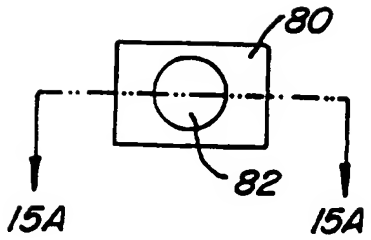

FIG. 15.

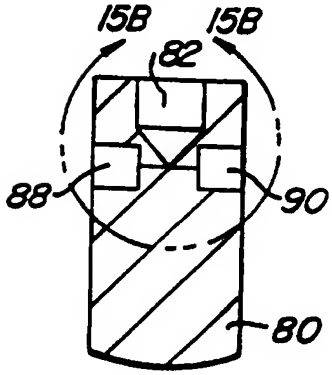

FIG. 15A

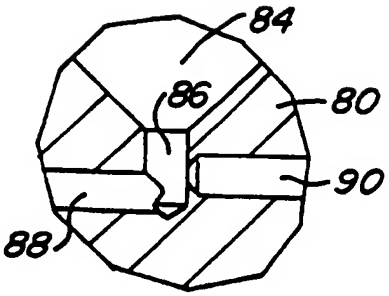

FIG. 15C.

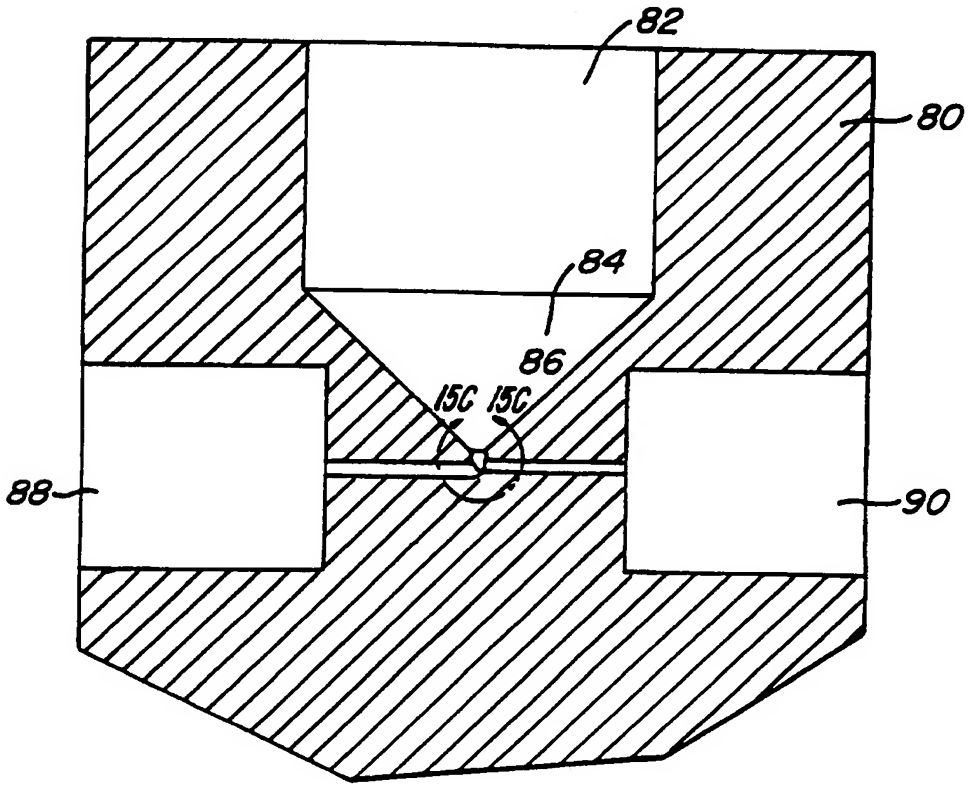

FIG. 15B.

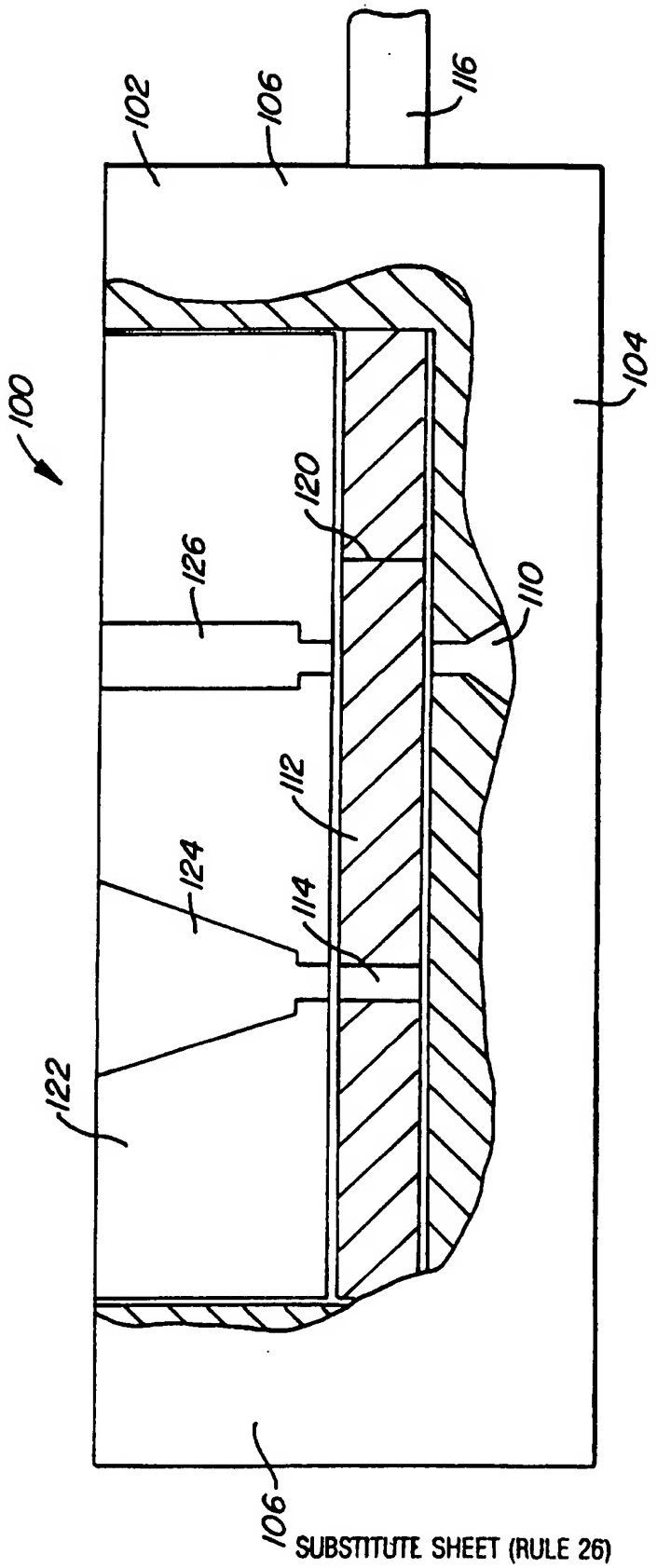

FIG. 16.

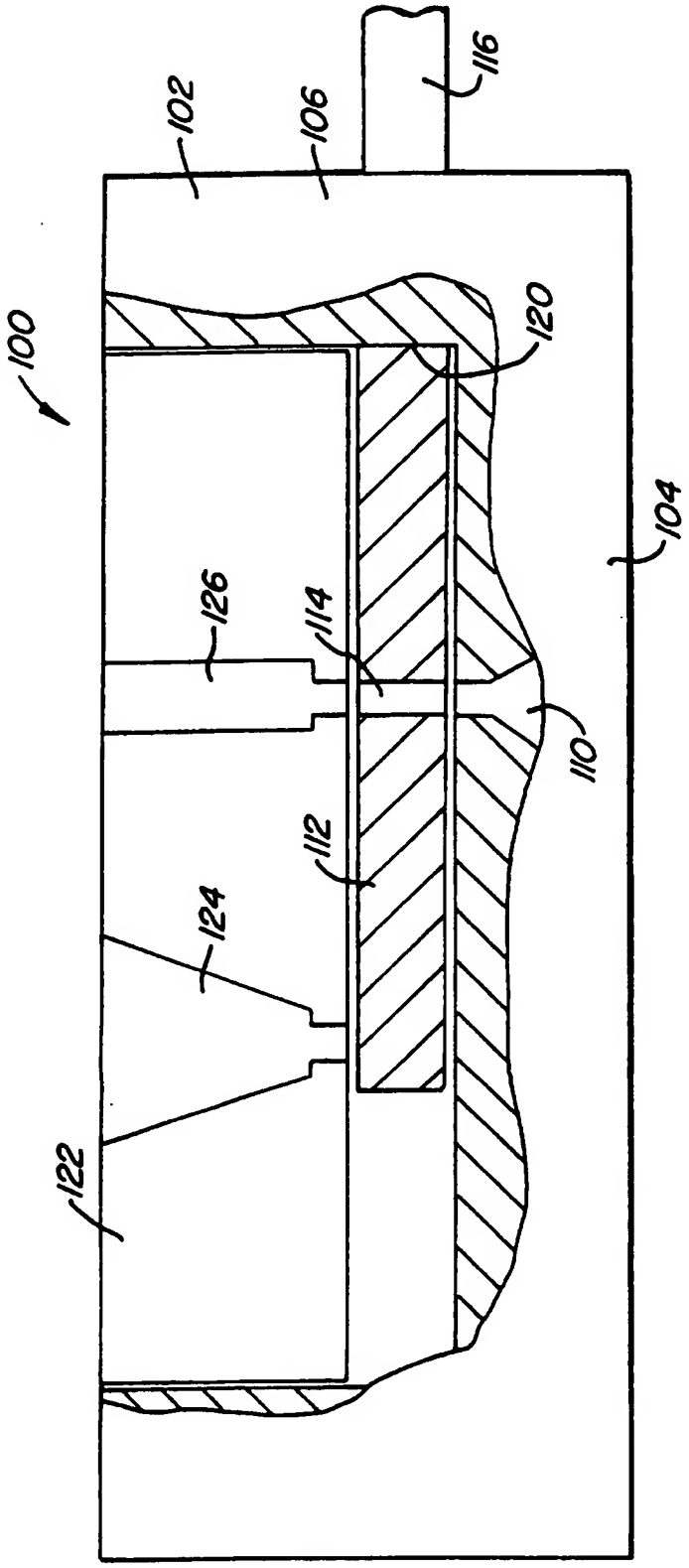

FIG. 17.

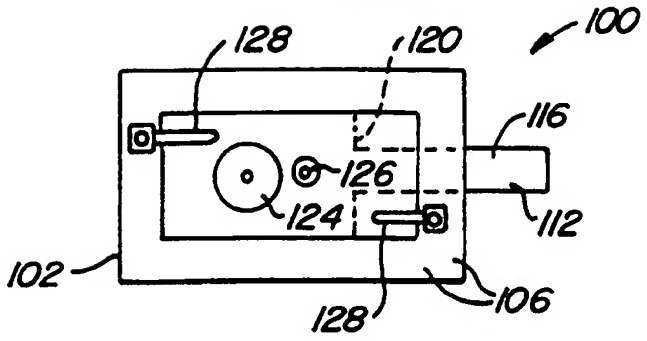

FIG. 18.

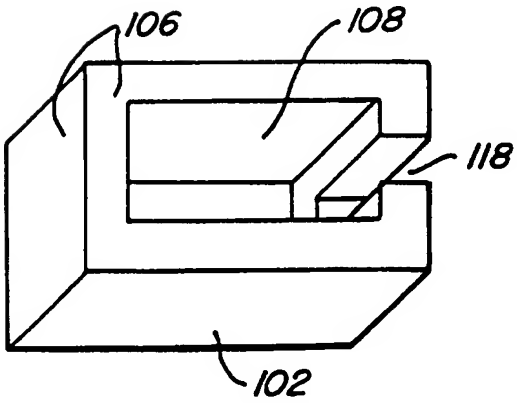

FIG. 19.

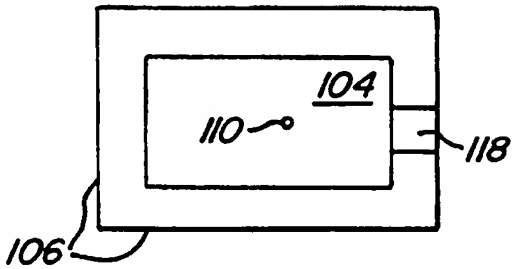

FIG. 20.

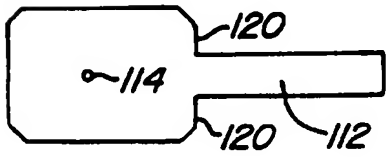

FIG. 21.

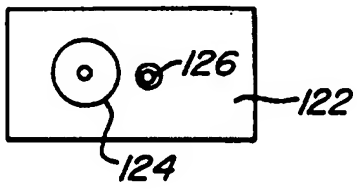

FIG. 22.

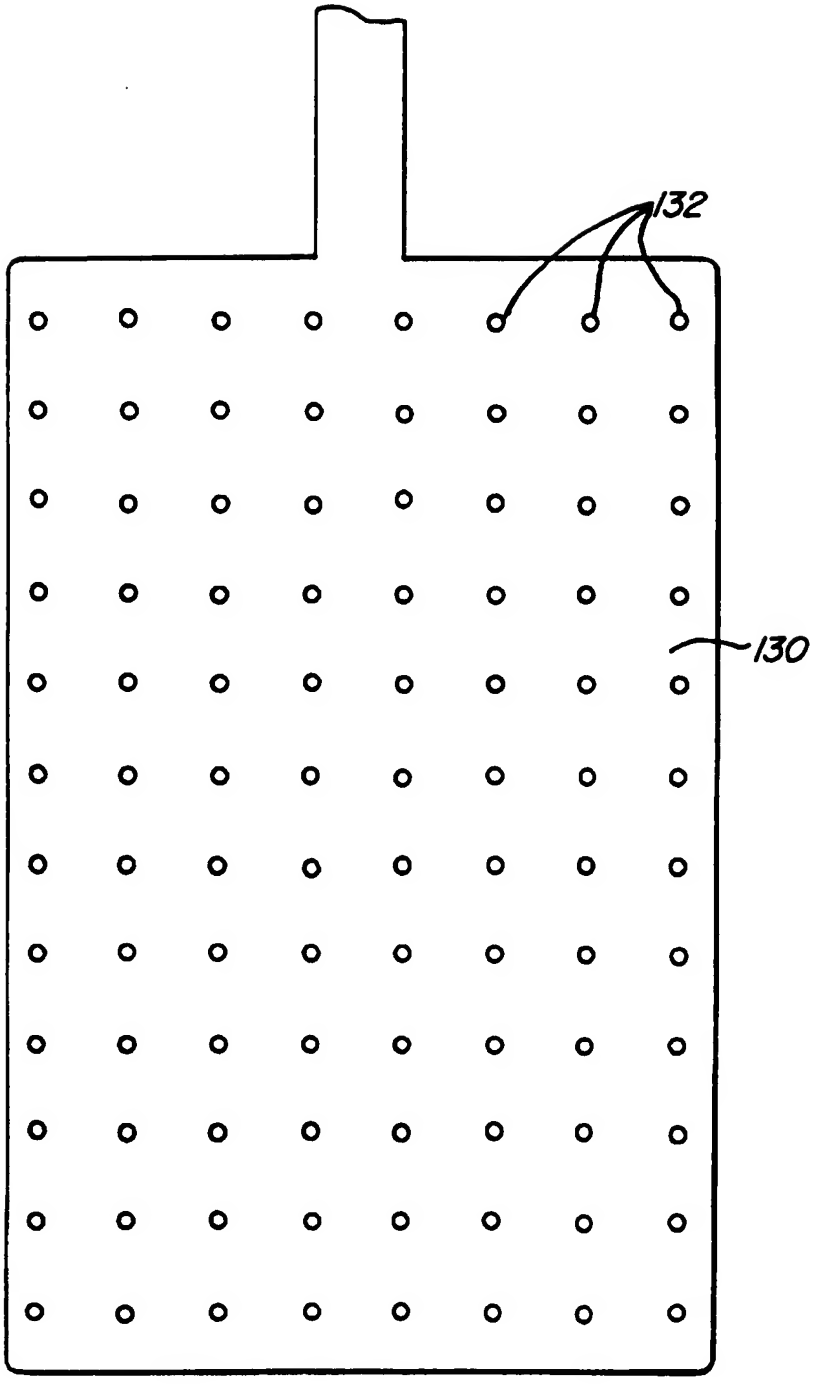

FIG. 23.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/17301

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :B65B 1/00
US CL :141/67
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 141/67, 9, 100, 105, 130; 221/233, 236

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, search terms: transporting, suspension, article, beads, pellets, dispens?, fill?, liquid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US, 4,328,189 A (HAESE et al.) 4 May 1982, col. 3, lines 23-58.	1, 7, 10, 16 ---------- 4, 14
Y	US 4,492,294 A (BALL) 8 January 1985, col. 2, lines 64-67.	4
Y	US 2,755,008 A (BELTZ et al.) 17 July 1956, col. 1, line 66, to col. 2, line 18.	14
X	US 4,650,093 A (MEYER-BOSSE) 17 March 1987, col. 3, line 42, to col. 4, line 24,	22, 27

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 20 NOVEMBER 1996	Date of mailing of the international search report 27 NOV 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer J. CASIMER JACYNA Telephone No. (703) 308-1113

Form PCT/ISA/210 (second sheet)(July 1992)*